



Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain:

Educational Pilot to improve care and safety with opioid treatment

Introduction:

This guideline is part of a year-long educational pilot to improve care and safety with opioid treatment for chronic non-cancer pain. It was developed by the Interagency Workgroup on Practice Guidelines¹ in collaboration with actively practicing physicians who specialize in pain management. This guideline does not apply to the treatment of cancer pain or end-of-life (hospice) care.

Providers prescribing opioids should be aware of the delicate balance between the undertreatment and overtreatment of chronic non-cancer pain. Because high dose opioid treatment can be ineffective and/or unsafe, providers must pay ongoing attention to adverse outcomes of chronic opioid use (Ballantyne 2003).

Recent studies indicate an increase in accidental deaths associated with the use of prescription opioids since 1999 (CDC 2005, Franklin 2005, Paulozzi 2006). At the same time, there has been a dramatic increase in the average daily morphine equivalent dose (MED) of the most potent (Schedule II) long acting opioids (Franklin 2005). In Washington State, the overall number of opioid-related deaths more than doubled between 1995 and 2004. There has also been a shift from non-prescription to prescription opioid-related deaths (Sabel 2006).

Part I: Guidelines for Initiating, Transitioning, and Maintaining Oral Opioids for Chronic Non-cancer pain

The purpose of Part I of this dosing guideline is to assist the primary care

provider who does not specialize in pain medicine in prescribing opioids for adults in a safe and effective manner:

- When instituting or transitioning opioid treatment from acute to chronic non-cancer pain;
- When assessing and monitoring opioid treatment for chronic non-cancer pain; and
- When weaning opioids if an opioid trial fails to yield improvements in function and pain.

See Part II of this dosing guideline for assistance in optimizing opioid treatment for patients whose morphine equivalent dose (MED) already exceeds 120 mg per day.

Dosing Threshold for Pain Consultation:

In order to improve the quality of care in the state of Washington, the state agencies, in collaboration with the physician panel, reviewed the available evidence and made the following recommendations:

- In general, the total daily dose of opioid should not exceed 120 mg of oral morphine equivalents for chronic non-cancer pain.
- Safety and effectiveness of opioid therapy for chronic non-cancer pain should be routinely evaluated.
- Although pain may be relieved at oral morphine doses up to 120 mg per day, pain relief may not be associated with psychological or functional improvement (Moulin 1996).
- A specialty consultation may be considered at any time if there is evidence of frequent adverse effects or lack of response to an opioid trial.
- Rarely, and only after pain management consultation, should the total daily dose of opioid be increased

¹ Department of Corrections, Health, Labor and Industries, Social and Health Services, and Health Care Authority

above 120 mg oral morphine equivalents.	
Up to 120mg/day MED (Cumulative daily dose when using more than one opioid. See Table 1 for specific opioid thresholds)	Above 120mg/day MED (Cumulative daily dose when using more than one opioid. See Table 1 for specific opioid thresholds)
<ul style="list-style-type: none"> No consultation needed if provider is documenting sustained improvement in function and pain. Consider specialty consultation if frequent adverse effects or lack of response is evident in order to address: <ul style="list-style-type: none"> ✓ Evidence of undiagnosed conditions; ✓ Presence of significant psychological condition affecting treatment; and ✓ Potential alternative treatments to reduce or discontinue use of opioids. 	<ul style="list-style-type: none"> Seek pain management consultation to address: <ul style="list-style-type: none"> ✓ Potential alternative treatments to opioids; ✓ Risk and benefit of a possible trial with opioid dose above 120mg/day MED; ✓ Assistance with ongoing documentation of improvement in function and pain; and ✓ Schedule for follow up with specialist if necessary.

Morphine Equivalent Dose Calculation:

For patients taking more than one opioid, the morphine equivalent doses of the different opioids must be added together to determine the cumulative dose. For example, if a patient takes six hydrocodone 5mg / acetaminophen 500mg and two 20mg oxycodone extended release tablets per day, the cumulative dose may be calculated as follows:

- 1) Hydrocodone 5mg x 6 tablets per day = 30mg per day.
- 2) Using the Equianalgesic Dose table on page 8 of this guideline, 30mg Hydrocodone = 30mg morphine equivalents.
- 3) Oxycodone 20mg x 2 tablets per day = 40mg per day.
- 4) Per Equianalgesic Dose table, 20mg oxycodone = 30mg morphine so 40mg oxycodone = 60mg morphine equivalents.
- 5) Cumulative dose is 30mg + 60mg = 90mg morphine equivalents per day.

An electronic opioid dose calculator can be downloaded at www.agencymeddirectors.wa.gov/guidelines.asp.

Consider Prescribing Opioids When:

- Other conservative measures have failed (e.g. NSAIDs, tricyclic antidepressants, and non-pharmacologic therapies) and opioids have not been tried.

- Patient has demonstrated sustained improvement in function and pain level in previous opioid trial.
- Patient has no relative contraindication to the use of opioids (e.g. active alcohol or other substance abuse).

Principles for Prescribing Opioids:

- Single prescriber
- Single pharmacy
- Patient and prescriber sign opioid agreement
- Lowest possible effective dose should be used
- Be cautious when using opioids with conditions that may potentiate opioid adverse effects (including COPD, CHF, sleep apnea, history of alcohol or substance abuse, elderly, or history of renal or hepatic dysfunction).
- Do not combine opioids with sedative-hypnotics, benzodiazepines or barbiturates for chronic, non-cancer pain unless there is a specific medical indication for the combination.
- Assess function and pain status (see *Part I: Tools for Assessing Function and Pain*).
- Monitor for medication misuse (see *Part II: Reasons to Discontinue Opioids or Refer for Addiction Management* for a list of drug-seeking behaviors).
- Random urine drug toxicology screening to objectively assure

compliance (see *Urine Drug Toxicology Screening*).

Instituting Opioid Treatment for Chronic, Non-cancer Pain:

Prior to initiating chronic opioid therapy, the provider should comprehensively assess the risks and benefits of treatment. The prescriber is responsible for routinely monitoring the safety and effectiveness of opioid therapy in providing pain relief and improving function. Both provider and patient should discuss and agree on:

- Risks and benefits of opioid therapy supported by an opioid agreement;
- Treatment goals and provider's established criteria to evaluate the effectiveness of opioid therapy; and
- A follow-up plan with specific time intervals to monitor treatment.

Treatment goals must include improvements in both function and pain while monitoring for and minimizing adverse effects (see *Part I: Principles for Prescribing Opioids*).

Depression and anxiety disorders are frequently associated with the use of opioids (Sullivan 2005). Extreme caution should be used and a specialty consultation is strongly encouraged prior to prescribing opioids when patients have a history of significant psychological conditions such as conversion disorder, somatization, borderline personality, mood disorder, PTSD, or history of alcohol or other substance abuse.

Transitioning Opioid Treatment from Acute Pain to Chronic, Non-cancer Pain:

- **Acute pain** is self-limiting and lasts from a few days to a few weeks following trauma or surgery.
- **Chronic pain** persists beyond the anticipated healing period for the specific disease condition.

The level of pain during an acute phase does not necessarily and accurately

predict the pain level in a chronic phase. Thus, opioid dosing for chronic treatment should be assessed and adjusted accordingly (see *Part I: Instituting Opioid Treatment for Chronic Non-cancer Pain*).

Tools for Assessing Function and Pain:

The key to effective opioid therapy for chronic non-cancer pain is sustained functional improvement (Loeser 1989, Devulder 2005). While there is no universally accepted tool to assess opioid treatment, it is important to use a tool that monitors both function and pain. An assessment of function should consistently measure the same elements to adequately determine the degree of progress. The following are functional assessment tools that may be helpful in monitoring your patient's progress:

- **SF36 Health Survey**
<http://www.npecweb.org/clinicaltoolbox.asp?id=26&selMenu=15,0>
- **QuickDash** for musculoskeletal disorders of the upper extremities
http://www.dash.iwh.on.ca/assets/images/pdfs/quickdash_q.pdf
- **Quality of Life Scale**
<http://www.npecweb.org/clinicaltoolbox.asp?id=26&selMenu=15,0>
- **Oswestry Disability Index**
http://www.chirogeek.com/001_Oswestry-Disability-level.htm
- **Neck Disability Index**
http://www.chirogeek.com/001_Neck-Disability-Index.htm
- **Short Musculoskeletal Function Assessment** (Swiontkowski 1999)

Assessing Effects of Opioid Treatment:

Opioid treatment is associated with the development of tolerance (White 2004). Evidence is accumulating that opioid treatment may also paradoxically induce abnormal pain sensitivity, including hyperalgesia and allodynia (Mao 2002, Ossipov 2005, King 2005). Thus, increasing opioid doses may not be the answer.

The provider should assess the risks and benefits of their patient's current opioid therapy. This assessment should include:

- Function and pain status (see *Part I: Tools for Assessing Function and Pain* a list of suggested tools);
- Possible adverse effects of current opioid doses;
- Potential psychological condition affecting treatment;
- Possible drug combinations or conditions that may potentiate opioid adverse effects (such as COPD, CHF, sleep apnea, history of alcohol or substance abuse, elderly, or history of renal or hepatic dysfunction); and
- Any relative contraindication to the use of opioids (active alcohol or other substance abuse, see *Part I: Urine Drug Toxicology Screening*, below).

If, after careful review of above considerations, no reasons for dose reduction or discontinuation are identified, and the provider feels (with support of objective measures of pain and function) that the patient is benefiting from current therapy, continuation at the effective opioid dose would be appropriate. Ongoing therapy, however, entails ongoing assessment. The above screening should be done on a regular basis to assess progression of therapy as the patient's condition changes over time.

Urine Drug Toxicology Screening:

Urine drug toxicology screening can improve the provider's ability to safely and appropriately manage opioid treatment. Urine toxicology can verify if the patient is taking the prescribed medications. It can also identify if other psychoactive tested substances are consumed, but not reported, which may impact the patient's safety, function and treatment. The NIDA 5 (National Institute on Drug Abuse) is the most commonly used basic urine drug test that screens for 5 common drug classes:

- Cannabinoids (marijuana, hash)
- Cocaine (crack)

- Amphetamines (methamphetamines, speed)
- Opioids (heroin, opium, codeine, morphine)
- Phencyclidine (PCP)

The NIDA 5 does not screen for many other drugs of abuse such as barbiturates, benzodiazepines, hydrocodone, methadone, oxycodone, propoxyphene, or other synthetic drugs. An expanded urine drug toxicology panel can be ordered to screen for these substances.

Positive results from a urine toxicology screen should be interpreted with caution. Over-the-counter medication may occasionally cause a positive result, particularly in the amphetamines and opioids classes. In some circumstances a positive result may require confirmatory tests and consultation with a certified Medical Review Officer (MRO). To locate a MRO in your area submit a search at the following website:

http://www.aamro.com/registry_search.html

Specialty Consultation:

Specialty consultation is recommended for ongoing severe pain symptoms with no improvement in function despite treatment with opioids. Consultation should address possible undiagnosed conditions, psychological conditions affecting treatment, and alternative treatments. The type of consultation obtained should be determined by the patient's presenting signs and symptoms. Consultation may be with, but not limited to, a physician specializing in psychiatry, neurology, anesthesiology, pain, physical medicine and rehabilitation, orthopedics, addiction medicine, rheumatology, or oncology.

Chronic opioid treatment can be challenging in patients with symptoms suggestive of mood, anxiety, and psychotic disorders. Consider psychiatric and/or psychological consultation for

intervention if a psychological condition is affecting treatment. Patients with signs of alcohol or other substance abuse should be referred to an addiction specialist (see *Part II: Referrals for Addiction Management or Opioid Agonist Treatment*).

Pain Management Consultation:

The provider should seek a pain management consultation for a possible trial with opioid doses above 120mg/day MED if there are no significant psychological issues or evidence of drug-seeking behaviors AND the patient has demonstrated improvement in function and pain level previously at a lower dose.

Consultation with a specialist does not necessitate transfer of the patient's care or on-going opioid prescribing. However, the consultant should advise the provider on a pain management plan that may include alternative treatments to reduce or discontinue use of opioids; adequate explanation of the risks and benefits of a possible trial with opioid dosing above 120mg/day MED; and the need for ongoing documentation of improvement in function and pain.

There are a number of organizations that offer credentialing or certification in pain medicine, although each organization has its own qualifying criteria and examination process. Credentialing or certification in pain medicine may be issued by one of the following organizations:

- American Board of Pain Medicine;
- American Board of Anesthesiology with certification of added qualifications in pain management;
- American Academy of Pain Management;
- American Board of Physical Medicine and Rehabilitation; and the
- American Board of Psychiatry and Neurology.

Weaning Opioids:

Not all patients benefit from opioids and a provider frequently faces the challenge of reducing the opioid dose or discontinuing the opioid altogether. From a **medical** standpoint, weaning from opioids can be done safely by slowly tapering the opioid dose, and taking into account the following issues:

- A decrease by 10% of the original dose per week is usually well tolerated with minimal physiological adverse effects. Some patients can be tapered more rapidly without problems (over 6 to 8 weeks).
- If opioid abstinence syndrome is encountered, it is rarely medically serious although symptoms may be unpleasant.
- Symptoms of an abstinence syndrome, such as nausea, diarrhea, muscle pain and myoclonus can be managed with clonidine 0.1 – 0.2 mg orally every 6 hours or clonidine transdermal patch 0.1mg/24hrs (Catapres TTS-1™) weekly during the taper while monitoring for often significant hypotension and anticholinergic side effects. In some patients it may be necessary to slow the taper timeline to monthly, rather than weekly dosage adjustments.
- Symptoms of mild opioid withdrawal may persist for six months after opioids have been discontinued.
- Consider using adjuvant agents, such as antidepressants to manage irritability, sleep disturbance or antiepileptics for neuropathic pain.
- Do not treat withdrawal symptoms with opioids or benzodiazepines after discontinuing opioids.
- Referral for counseling or other support during this period is recommended if there are significant behavioral issues.
- Referral to a pain specialist or chemical dependency center should be made for complicated withdrawal symptoms.

Recognizing and Managing Behavioral Issues during Opioid Weaning:

Opioid tapers can be done safely and do not pose significant health risks to the patient. In contrast, extremely challenging behavioral issues may emerge during an opioid taper (Passik 2006).

Behavioral challenges frequently arise in the setting of a provider who is tapering the opioid dose and a patient who places great value on the opioid he/she is receiving. In this setting, some patients will use a wide range of interpersonal strategies to derail the opioid taper. These may include:

- Guilt provocation (“You are indifferent to my suffering”);
- Threats of various kinds; or
- Exaggeration of their actual suffering in order to disrupt the progress of a scheduled taper.

There are no fool-proof methods for preventing behavioral issues during an opioid taper, but strategies implemented at the beginning of the opioid therapy are most likely to prevent later behavioral problems if an opioid taper becomes necessary (see *Part I: Instituting Opioid Treatment for Chronic Non-cancer Pain*).

Part II: Guidelines for Optimizing Treatment with Opioid Doses Greater than 120 mg MED per day

The purpose of Part II of this dosing guideline is to assist the provider in optimizing opioid treatment:

- When assessing effectiveness of therapy in patients whose total morphine equivalent dose exceeds 120 mg per days;
- When reducing the total daily opioid dose; and
- When discontinuing opioid therapy.

Assessing Effects of Opioid Doses Greater than 120 mg MED per day:

As previously stated, ongoing opioid treatment requires ongoing assessment to optimize therapy. This is important in light of the development of hyperalgesia and other abnormal pain sensitivity with

chronic high dose opioid treatment. If, after using the guidelines from *Part I: Assessing Effects of Opioid Treatment*, the prescriber feels that current treatment is not benefiting the patient, a dose reduction or discontinuation is warranted. However, if current treatment is benefiting the patient as demonstrated by objective measures of pain and function, it may be appropriate to continue while establishing a plan to monitor therapy as the patient's condition changes over time (see *Part I: Principles for Prescribing Opioids*).

How to Reduce and Reassess at Lower Opioid Doses:

Treatment with opioids, even at high doses, does not guarantee freedom from chronic pain and some patients may actually do better on lower doses of opioids (Mao 2002, Ballantyne 2003). A decrease by 10% of the original dose per week is usually well tolerated. Behavior issues or physical withdrawal symptoms can be a major obstacle to an otherwise beneficial dose reduction (see *Part I: Weaning Opioids and Recognizing and Managing Behavioral Issues during Opioid Weaning*).

The provider should assess the patient's status after discontinuing or reducing the opioid doses to less than 120mg MED per day. If the chosen assessment tool indicates improved patient status, other than subjective pain complaints, or if there is improvement in opioid-related side effects, maintain the patient off opioids or at the new reduced dose and reassess at a later time.

Conversely, if there is evidence of functional and symptomatic deterioration following opioid taper, the provider can resume prior dosing or strongly consider consulting with a pain management specialist to evaluate additional therapeutic options.

Referrals to Pain Centers:

A referral for counseling or other support during opioid taper or dose reduction is

recommended if there are significant behavior issues. In addition, a multidisciplinary pain program may be considered when appropriate to address the psychosocial and cognitive aspects of chronic pain together with patients' physical rehabilitation (Guzman 2002).

Recognizing Aberrant Behaviors during Opioid Treatment:

Patients who exhibit aberrant behaviors may or may not be at risk for opioid abuse. There is no universally accepted screening tool to predict aberrant behaviors with opioid treatment for chronic pain. However, it is important to identify aberrant behaviors as they can affect the medical management of your patients (see *Part II: Reasons to Discontinue Opioids or Refer for Addiction Management*).

Patients with a co-morbid psychiatric condition or addiction are at higher risk of uncontrolled opioid use despite their attempts to follow the treatment plan (Streltzer 2001, Streltzer 2006, Passik 2006). Providers should seek a consultation with an addiction specialist if there is co-morbid substance dependence or abuse.

Reasons to Discontinue Opioids or Refer for Addiction Management:

- **NO** improvement in function and pain after a sufficient opioid trial;
- Patient exhibits drug-seeking behaviors or diversion:
 - Selling prescription drugs
 - Forging prescriptions
 - Stealing or borrowing drugs
 - Frequently losing prescriptions
 - Aggressive demand for opioids
 - Injecting oral/topical opioids
 - Unsanctioned use of opioids
 - Unsanctioned dose escalation
 - Concurrent use of illicit drugs
 - Failing a drug screen
 - Getting opioids from multiple prescribers

Referrals for Addiction Management or Opioid Agonist Treatment:

A patient who exhibits overt signs of alcohol or substance use disorder as defined in the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM IV) should be referred to an addiction specialist for appropriate treatment. Prognosis is poor for patients with a DSM IV diagnosis of opioid dependence (304.00) or opioid abuse (305.50) who do not receive opioid agonist therapy, such as methadone or buprenorphine (Sees 2000, Kakko 2003).

Methadone can only be provided to treat a DSM IV diagnosis of opioid dependence through a federally licensed opioid treatment program (OTP). A referral for treatment may be made to any one of the licensed OTPs in Washington State:

- <http://www1.dshs.wa.gov/DASA/services/certification/GB.shtml> and click on Appendix Q.

Buprenorphine or buprenorphine/naloxone may also be prescribed by a qualified physician to treat opioid addiction. Any pharmacy can fill a buprenorphine or buprenorphine/naloxone prescription. To find qualified physicians in Washington, access:

- http://buprenorphine.samhsa.gov/bwns_locator/dr_search.htm

Additional Resources:

- DSHS Tool Kit to help address drug and alcohol issues in Medicaid patients (access <http://maa.dshs.wa.gov/pharmacy/Toolkit.htm>)
- Division of Alcohol and Substance Abuse (DASA) at 877-301-4557
- List of providers for pain management consultation www.agencymeddirectors.wa.gov/guidelines.asp
- Collaborative Opioid Prescribing Education (COPE) UW CME <http://depts.washington.edu/cme/online/>

FINAL DRAFT

Table 1: Dosing Threshold for Selected Opioids*

Opioid	Recommended Dose Threshold for Pain Consult (NOT Equianalgesic)	Recommended Starting Dose for Opioid-naïve patients	Considerations
Codeine	800mg per 24 hours	30mg q 4-6 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See Acetaminophen Warning.
Fentanyl Transdermal	50mcg/hour (q 72 hr)		Use only in opioid-tolerant patients who have been taking ≥ 60mg MED daily for a week or longer
Hydrocodone	120mg per 24 hours	5-10mg q 4-6 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See Acetaminophen Warning.
Hydromorphone	30mg per 24 hours	2mg q 4-6 hours	
Methadone	40mg per 24 hours	2.5-5mg BID - TID	Methadone is difficult to titrate due to its half-life variability. It may take a long time to reach a stable level in the body. Methadone dose should not be increased more frequently than every 7 days. Do not use as PRN or combine with other LA opioids.
Morphine	120mg per 24 hours	Immediate-release: 10mg q 4 hours	Adjust dose for renal impairment.
		Sustained-release: 15mg q 12 hours	
Oxycodone	80mg per 24 hours	Immediate-release: 5mg q 4-6 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See Acetaminophen Warning.
		Sustained Release: 10mg q 12 hours	
Oxymorphone	40mg per 24 hours	Immediate-release: 5-10mg q 4-6 hours	Use with extreme caution due to potential fatal interaction with alcohol or medications containing alcohol.
		Sustained Release: 10mg q 12 hours	

*Meperidine and propoxyphene products should not be prescribed for chronic, non-cancer pain.

Acetaminophen Warning with Combination Products:

Hepatotoxicity can result from prolonged use or doses in excess of recommended maximum total daily dose of acetaminophen (including over the counter products).

- Short-term use (<10 days) – 4000 mg/day
- Long-term use – 2500mg/day

Some key considerations in dosing long acting opioids are:

- Monitoring for adequate analgesia and use of “rescue” medications (at least until the long-acting opioid dose is stabilized). All new dosage calculations should include consideration for concurrent utilization of short-acting opioids.
- If the patient is more debilitated, frail and/or has significant metabolic impairments (e.g. renal or hepatic dysfunction), consider starting at the lower end of the conversion dose range.
- Always monitor for adverse effects (nausea, constipation, oversedation, itching, etc.)

Equianalgesic Dose Table for Converting Opioid Therapies

All conversions between opioids are estimates generally based on “equianalgesic dosing” or ED. Patient variability in response to these EDs can be large, due primarily to genetic factors and incomplete cross-tolerance. **It is recommended that, after calculating the appropriate conversion dose, that it be reduced by 25-50% to assure patient safety.**

Opioid	Approximate Equianalgesic Dose (oral & transdermal)*
Codeine	200mg
Fentanyl transdermal	12.5mcg/hr
Hydrocodone	30mg
Hydromorphone	7.5mg
Methadone	Chronic: 4mg**
Morphine	30mg
Oxycodone	20mg
Oxymorphone	10mg

*Adapted from VA 2003 & FDA labeling

**Equianalgesic dosing ratios between methadone and other opioids are complex, thus requiring slow, cautious conversion (Ayonrinde 2000).

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